Fig. 1A

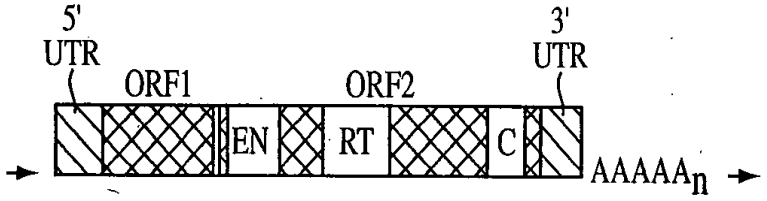

5'
UTR
ORF1
ORF2
3'
UTR
EN
RT
C
AAAAA$_n$

Fig. 1B

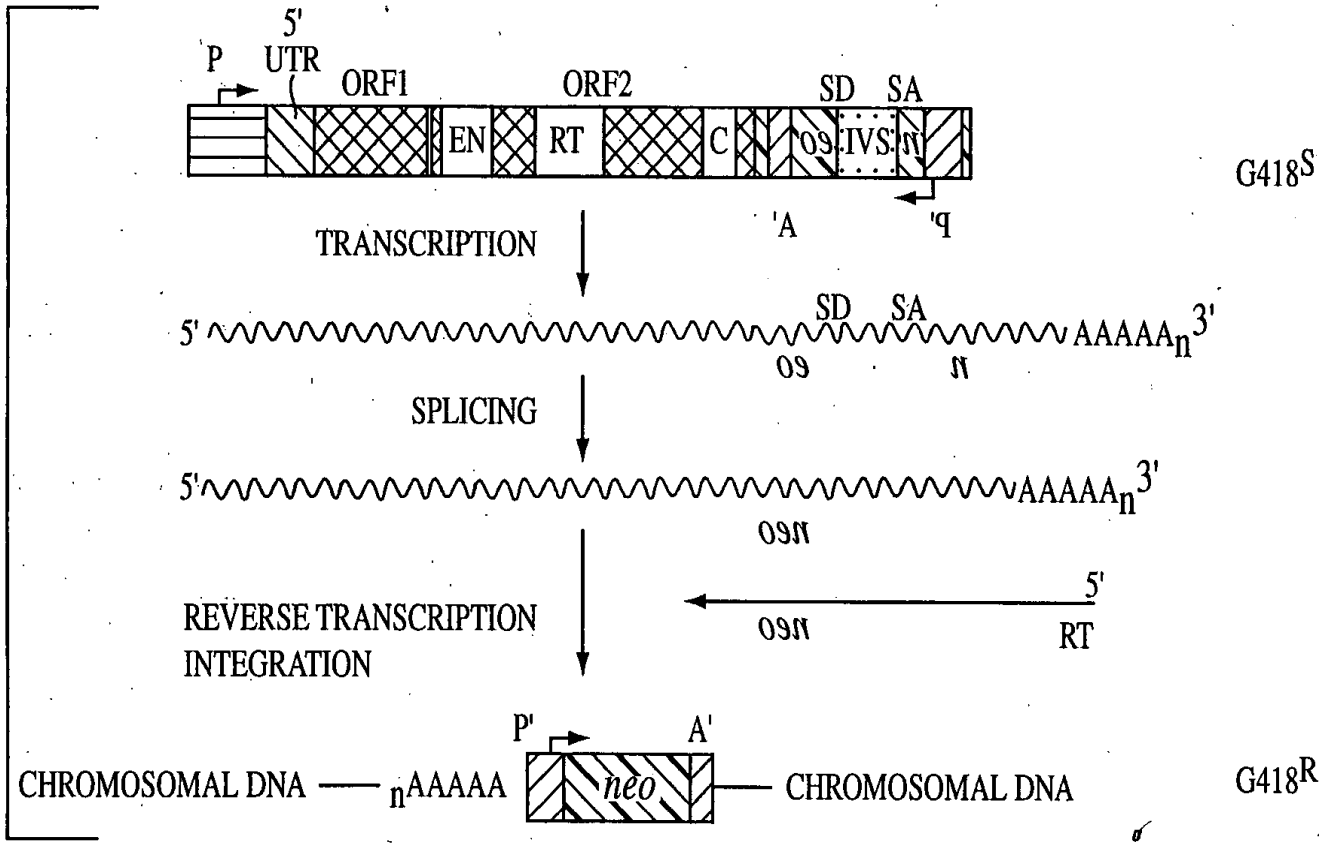

5'
P
UTR
ORF1
ORF2
SD
SA
EN
RT
C
IVS
G418^S
TRANSCRIPTION
SD
SA
5'
AAAAA$_n$ 3'
SPLICING
5'
AAAAA$_n$ 3'
REVERSE TRANSCRIPTION
INTEGRATION
5'
RT
P'
A'
CHROMOSOMAL DNA
$_n$AAAAA
neo
CHROMOSOMAL DNA
G418^R

Fig. 2A

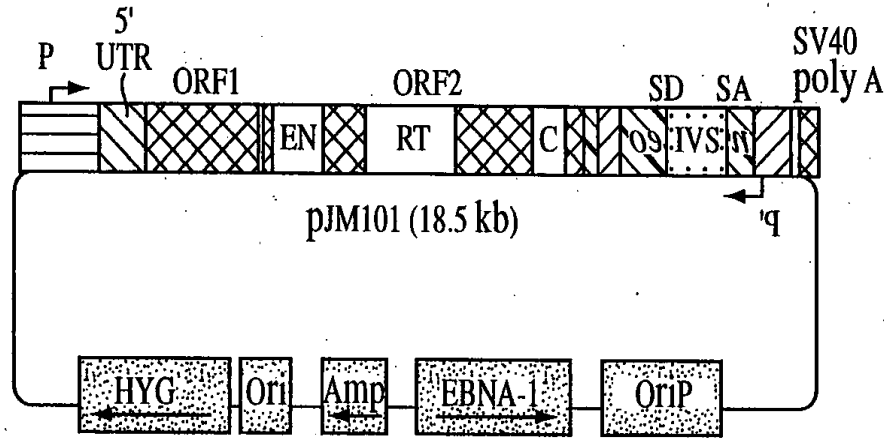


Fig. 2Bi

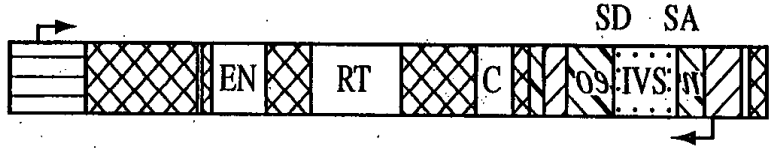


Fig. 2Bii

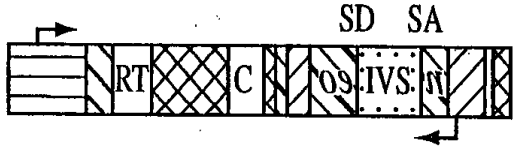
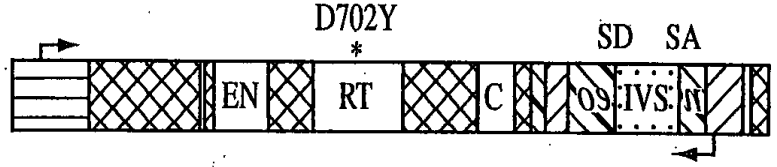


Fig. 2Biii



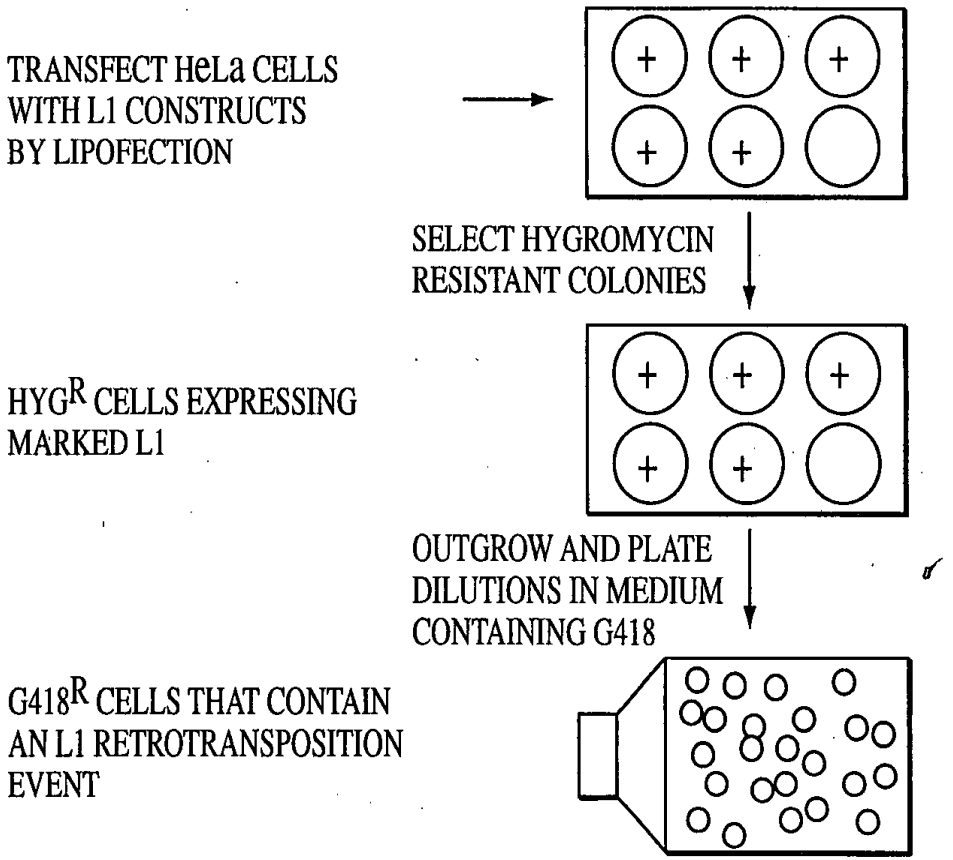

TRANSFECT HeLa CELLS
WITH L1 CONSTRUCTS
BY LIPOFECTION
SELECT HYGROMYCIN
RESISTANT COLONIES
HYG^R CELLS EXPRESSING
MARKED L1
OUTGROW AND PLATE
DILUTIONS IN MEDIUM
CONTAINING G418
G418^R CELLS THAT CONTAIN
AN L1 RETROTRANSPOSITION
EVENT

Fig. 3A

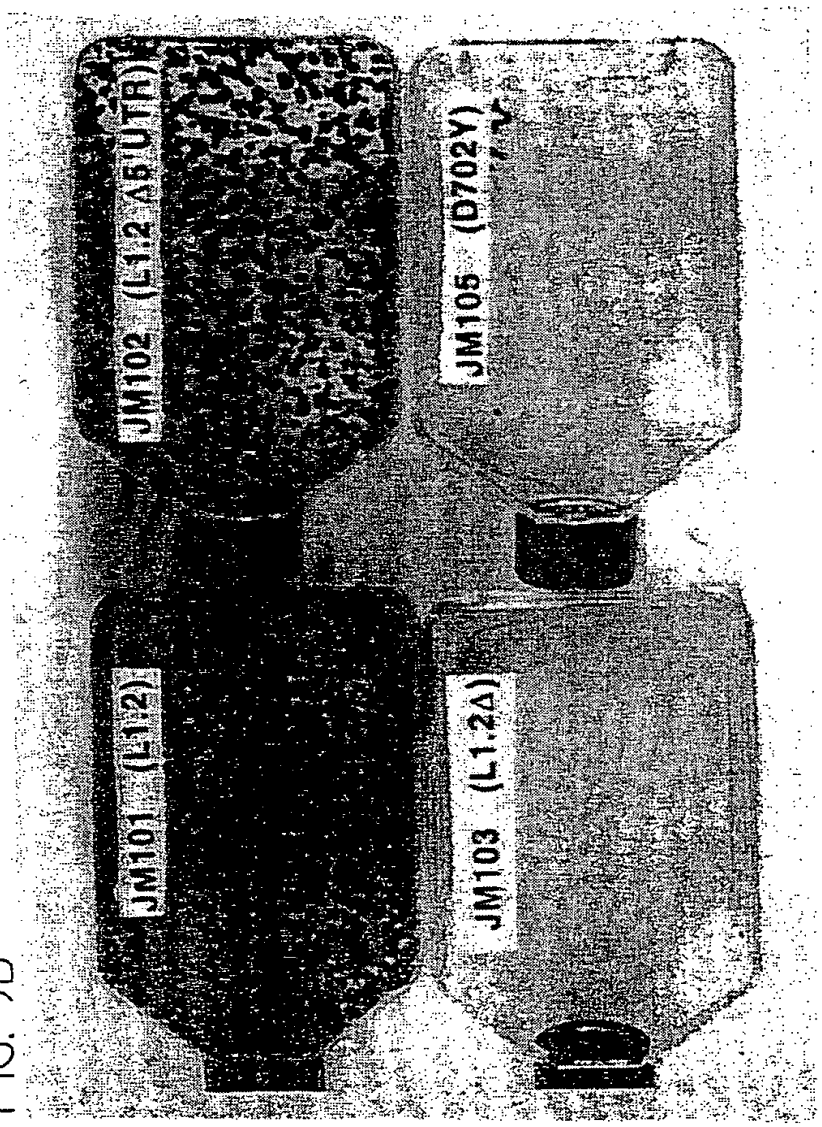


FIG. 3B

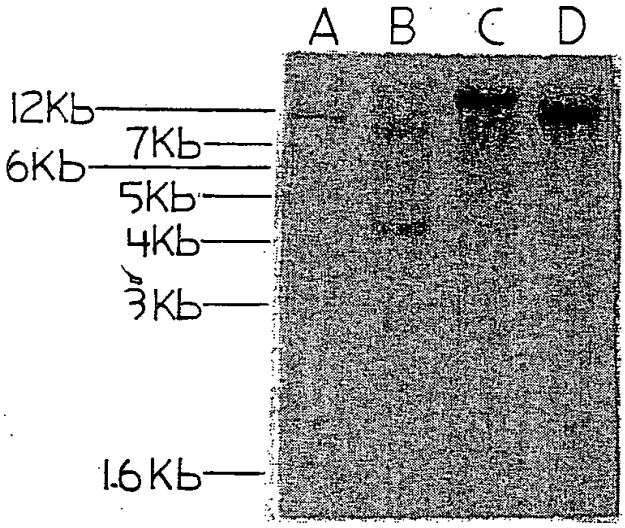


FIG.4A

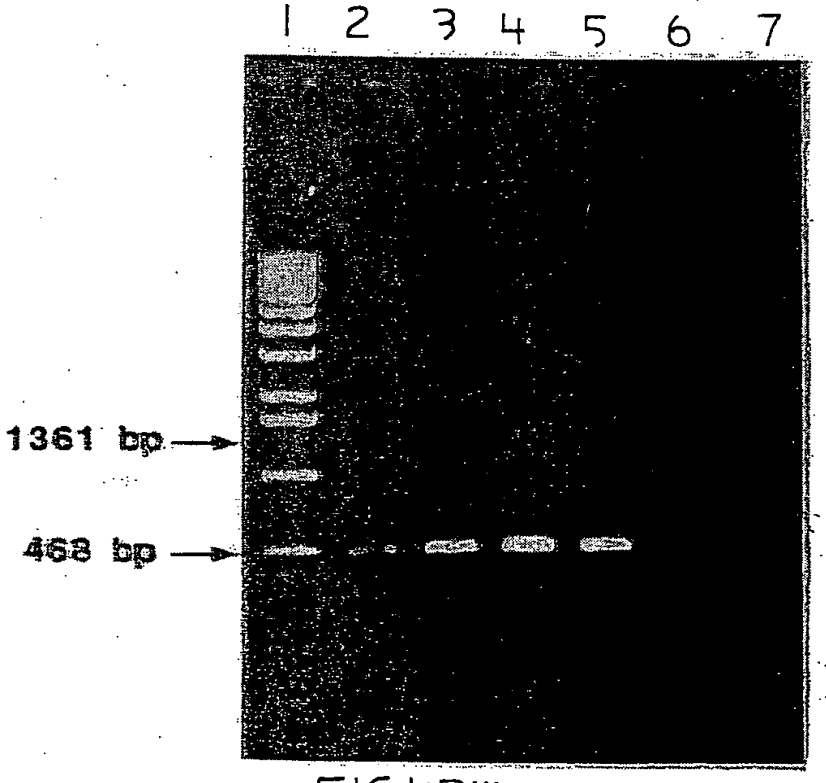


FIG.4Biii

Fig. 4Bi

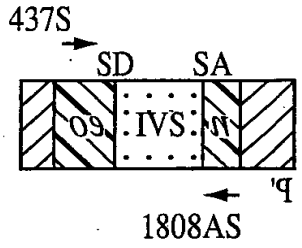
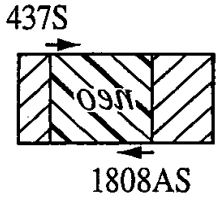


Fig. 4Bii



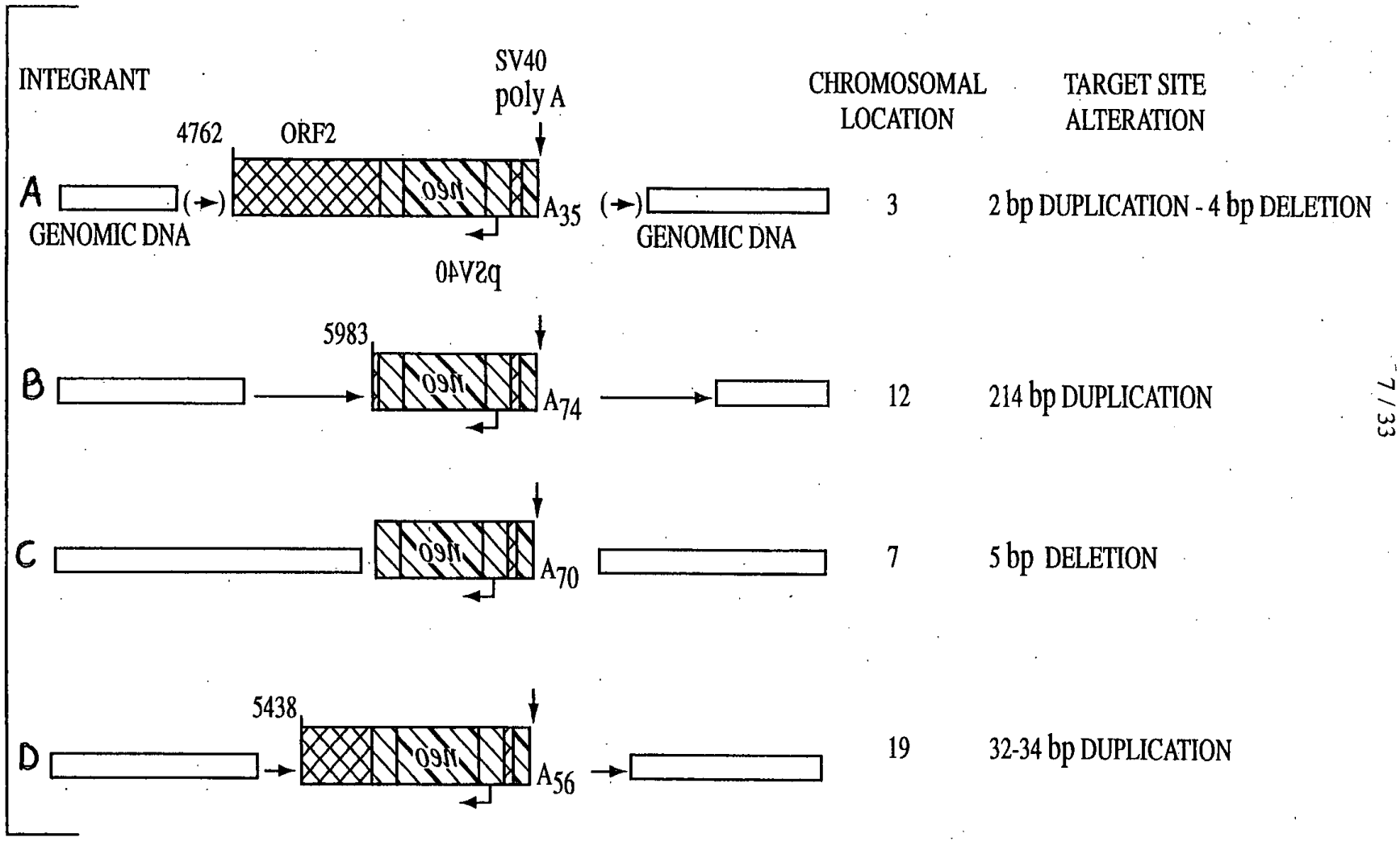

INTEGRANT
SV40
poly A
CHROMOSOMAL LOCATION
TARGET SITE ALTERATION
4762
ORF2
A
GENOMIC DNA
A35
GENOMIC DNA
3
2 bp DUPLICATION - 4 bp DELETION
5983
B
A74
12
214 bp DUPLICATION
C
A70
7
5 bp DELETION
5438
D
A56
19
32-34 bp DUPLICATION

Fig. 5

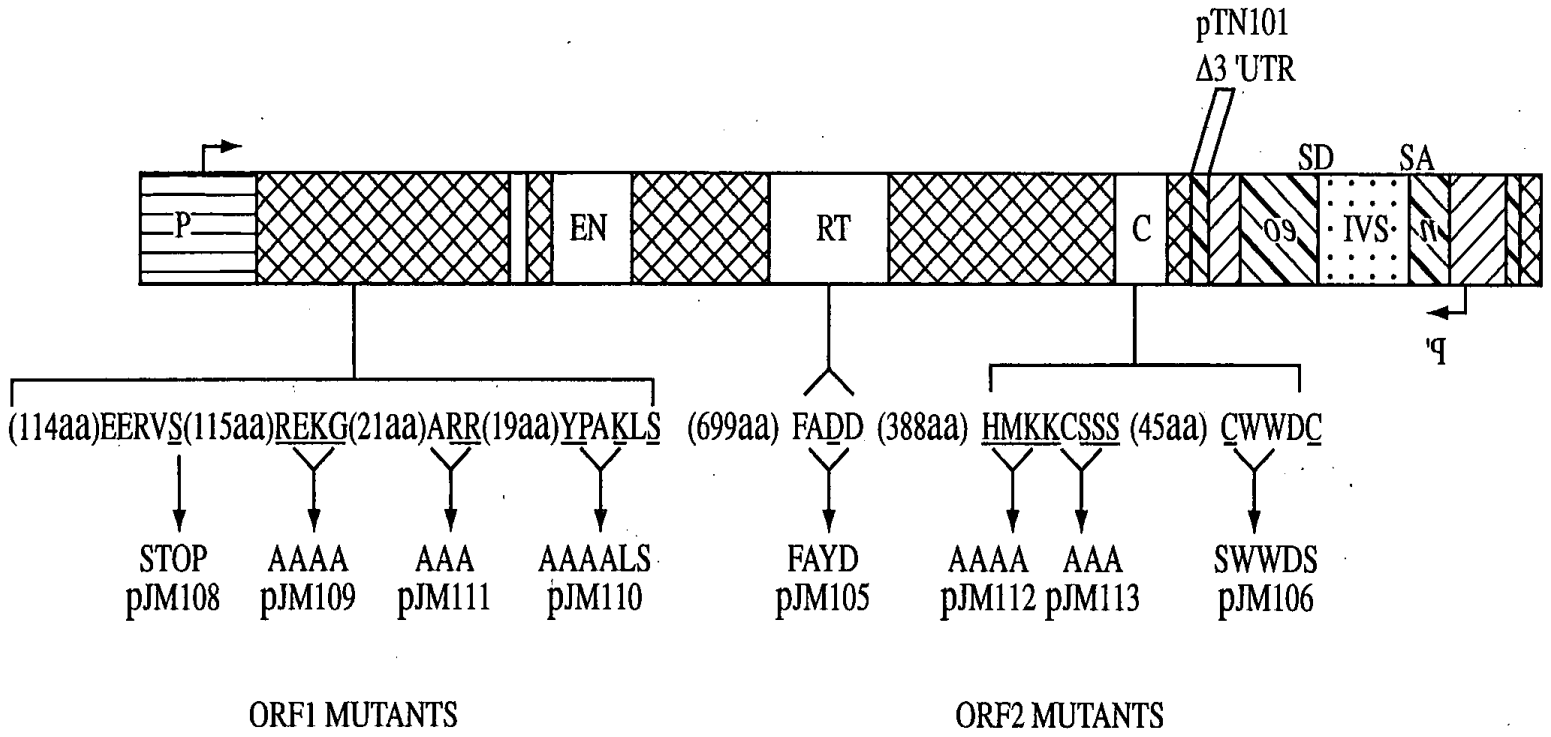

pTN101
Δ3 'UTR
SD
SA
P
EN
RT
C
IVS
(114aa)EERVS(115aa)REKG(21aa)ARR(19aa)YPAKLS
(699aa) FADD (388aa) HMKKCSSS (45aa) CWWDC
STOP
pJM108
AAAA
pJM109
AAA
pJM111
AAAALS
pJM110
FAYD
pJM105
AAAA
pJM112
AAA
pJM113
SWWDS
pJM106
ORF1 MUTANTS
ORF2 MUTANTS

Fig. 6

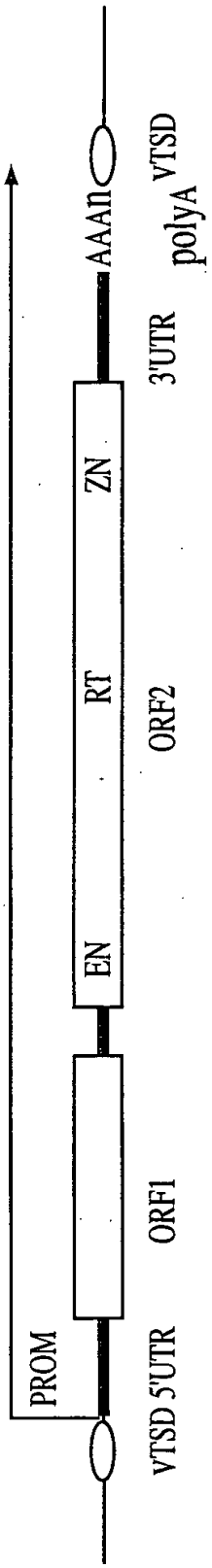


Fig. 7A

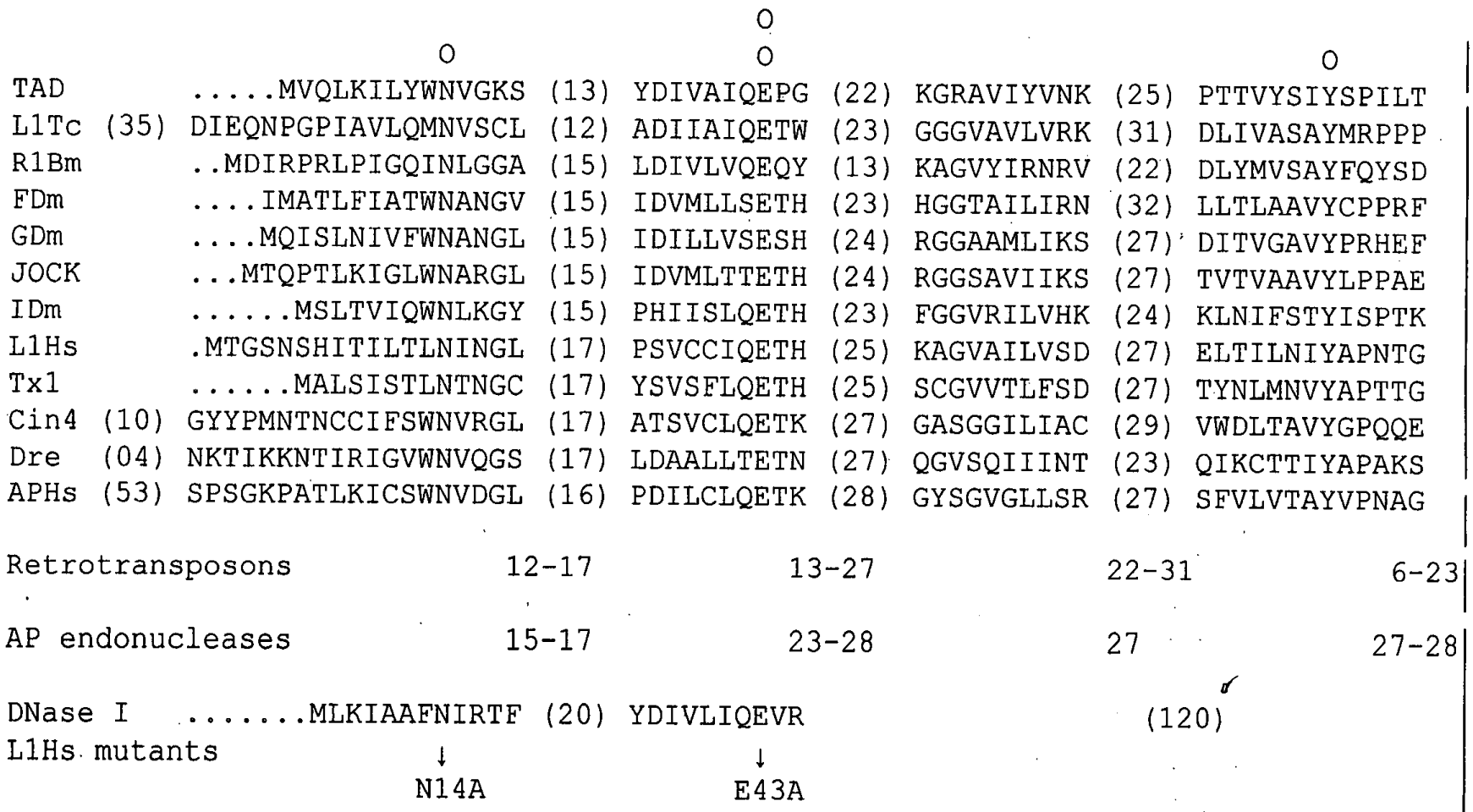


FIG. 7Bi

FIG. 7

FIG. 7Bi	FIG. 7Bii

```
                                                  O             O
          O O                     O               O            OOO
(23) NLVAVGDLNLHHPDWD (29) GE.PTRLGNATRGERDGTIDHAWLS (16) GSDHCPQEIWVQV
(17) PLLLCGDFNMHHPQWE (25) GE.ITTARGTRER...SCIDLTWSK (13) LSDHYVLTFTLHQ
(19) RVVICADTNAHSPLWH (35) GHLPTFSTANGE....SYVDVTLST (14) SSDHRLIVFGVGG
(16) HFIAAGDYNAKHTHWG (26) PGSPTYWPSDLN.KLPDLIDFAVTK (15) SSDHSPVLIHLRR
(16) RFIAAGDFNAKHSWWG (24) TGEPTHWPSDPS.KQPDLLDIAICK (15) VSDHSAVNLLLNI
(16) KFIAGGDYNAKHAWWG (24) TGEPTFYSYNPL.LTPSALDFFITC (15) SSDHLPILAVLHA
(16) PSLITGDFNGWHPSWG (24) DKSPTHFSTH...NTYSHIDLTLCS (16) GSDHFPIITTLFP
(18) HTLIMGDFNTPLSTLD (34) TE.YTF..FSAPHHTYSKIDHIVGS (16) LSDHSAIKLELRI
(21) ALIIGGDFNYTLDARD (34) VA.FTYVRVRDGHVSQSRIDRIYIS (16) FSDHNCVSLRMSI
(19) EWLILGDFNMIRRVGE (30) KK.FT.WSNEQDDPTMSRIDRLMAT (18) TSDHSPLLMQGHS
(17) SDIITGDFNVDCSVDN (19) NG.ITFPR......NKSTIDRVFVS (17) KSDHNMVIIELKI
(27) PLVLCGDLNVAHEEID (45) TF.WTYMMNARSKNVGWRLDYFLLS (17) GSDHCPITLYLAL

                  21-35                          13-18

                  44-50                          17-21

DVMLMGDFNADCSYVT (31) ................CAYDRIVVA (31) ISDHYPVEVTLT
      ↓                                    ↓            ↓
    D145A                                D205G        H230A
```

FIG. 7Bii

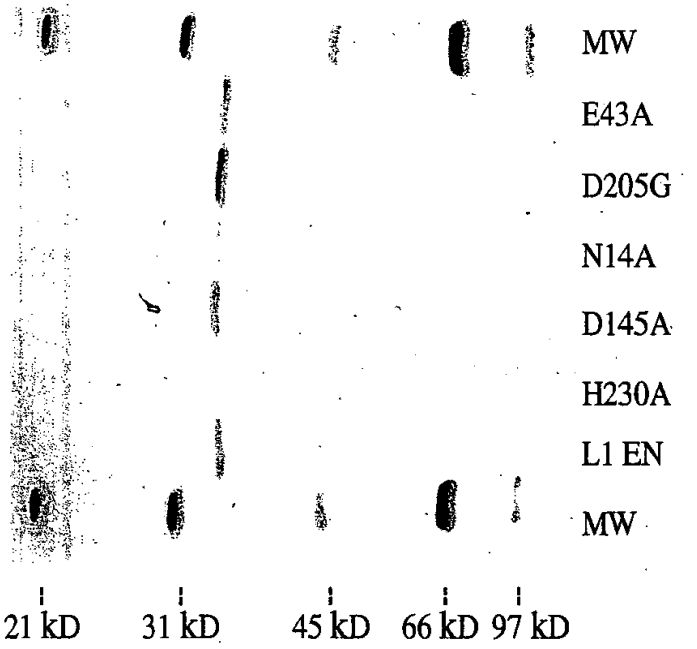

MW
E43A
D205G
N14A
D145A
H230A
L1 EN
MW
21 kD
31 kD
45 kD
66 kD
97 kD

Fig. 8A

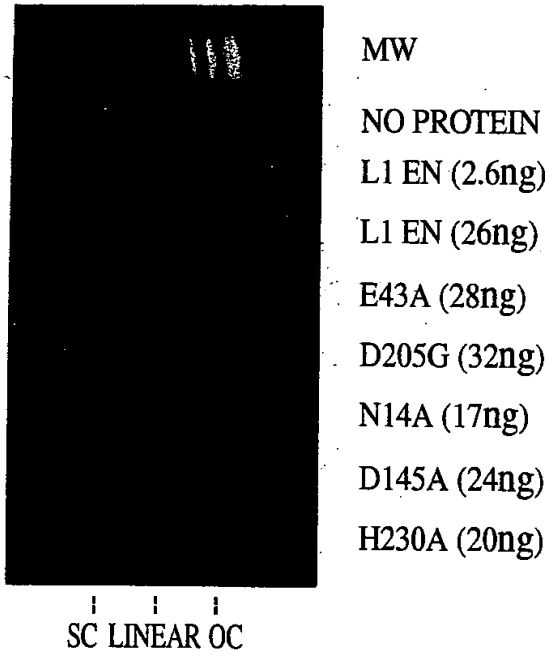

MW
NO PROTEIN
L1 EN (2.6ng)
L1 EN (26ng)
E43A (28ng)
D205G (32ng)
N14A (17ng)
D145A (24ng)
H230A (20ng)
SC LINEAR OC

Fig. 8B

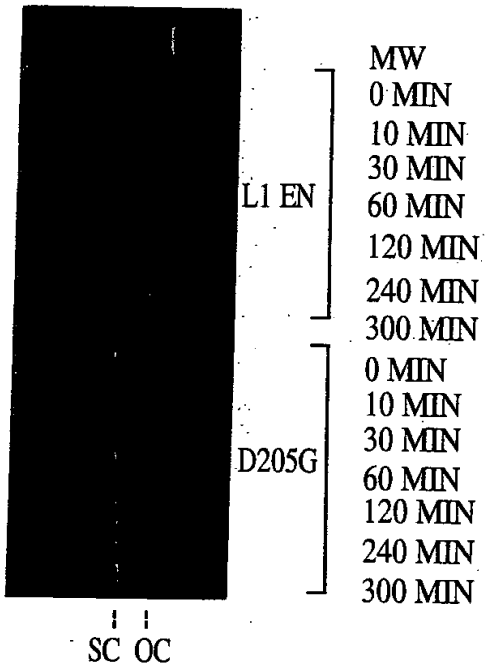

MW
0 MIN
10 MIN
30 MIN
60 MIN
120 MIN
240 MIN
300 MIN
L1 EN
0 MIN
10 MIN
30 MIN
60 MIN
120 MIN
240 MIN
300 MIN
D205G
SC OC

Fig. 8C

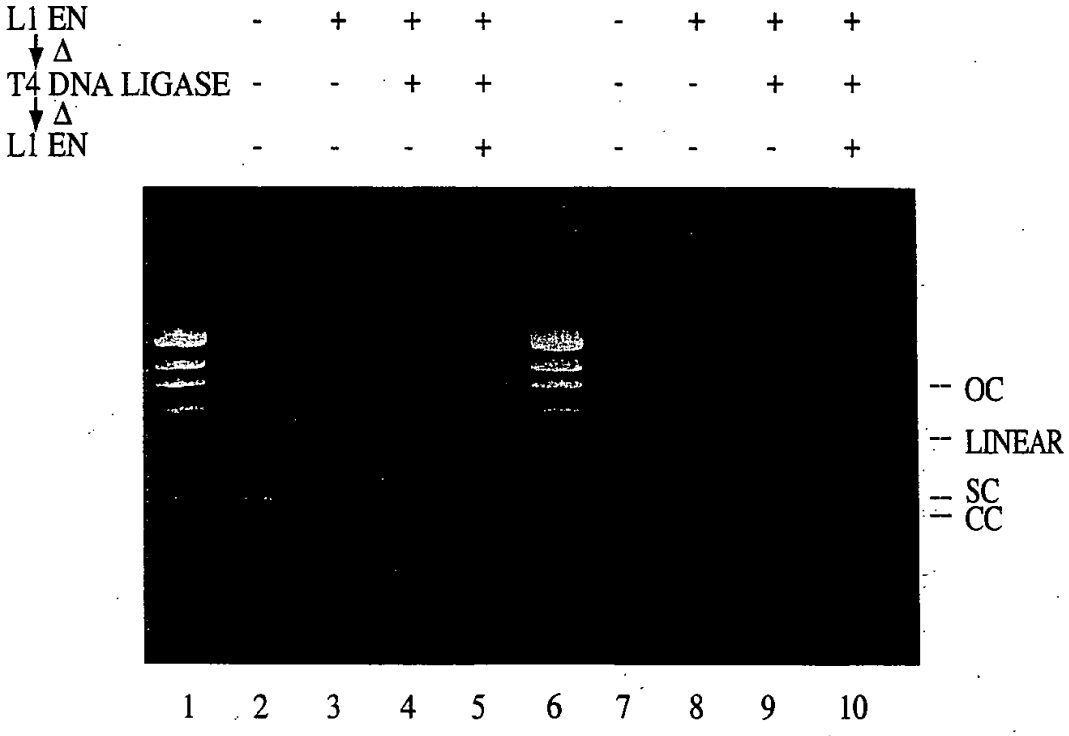

L1 EN - + + + - + + +
Δ
T4 DNA LIGASE - - + + - - + +
Δ
L1 EN - - - + - - - +
OC
LINEAR
SC
CC
1 2 3 4 5 6 7 8 9 10

Fig. 9

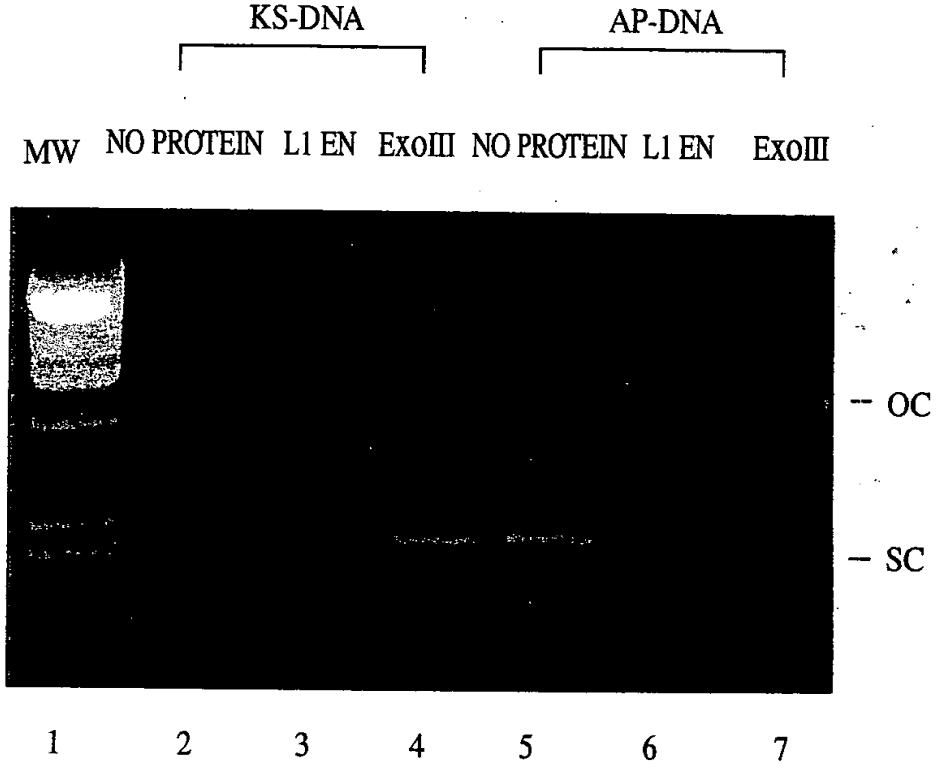


Fig. 10

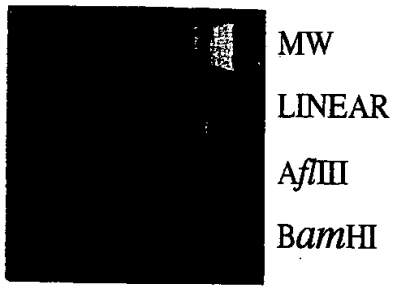


Fig. 11A

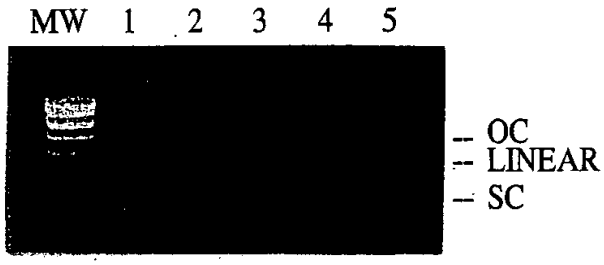


Fig. 11B

Fig. 11Ci Fig. 11Cii Fig. 11Ciii

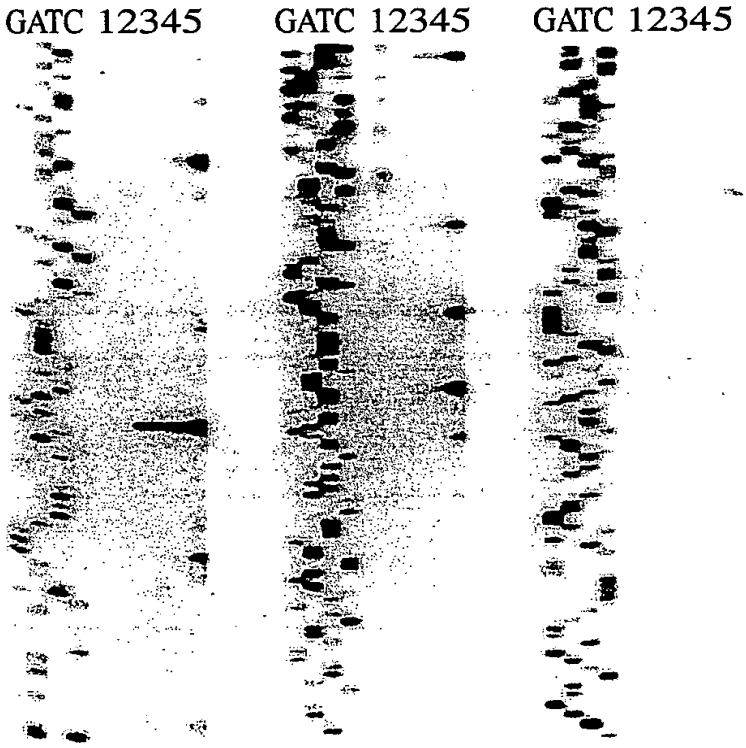


FIG. 11D

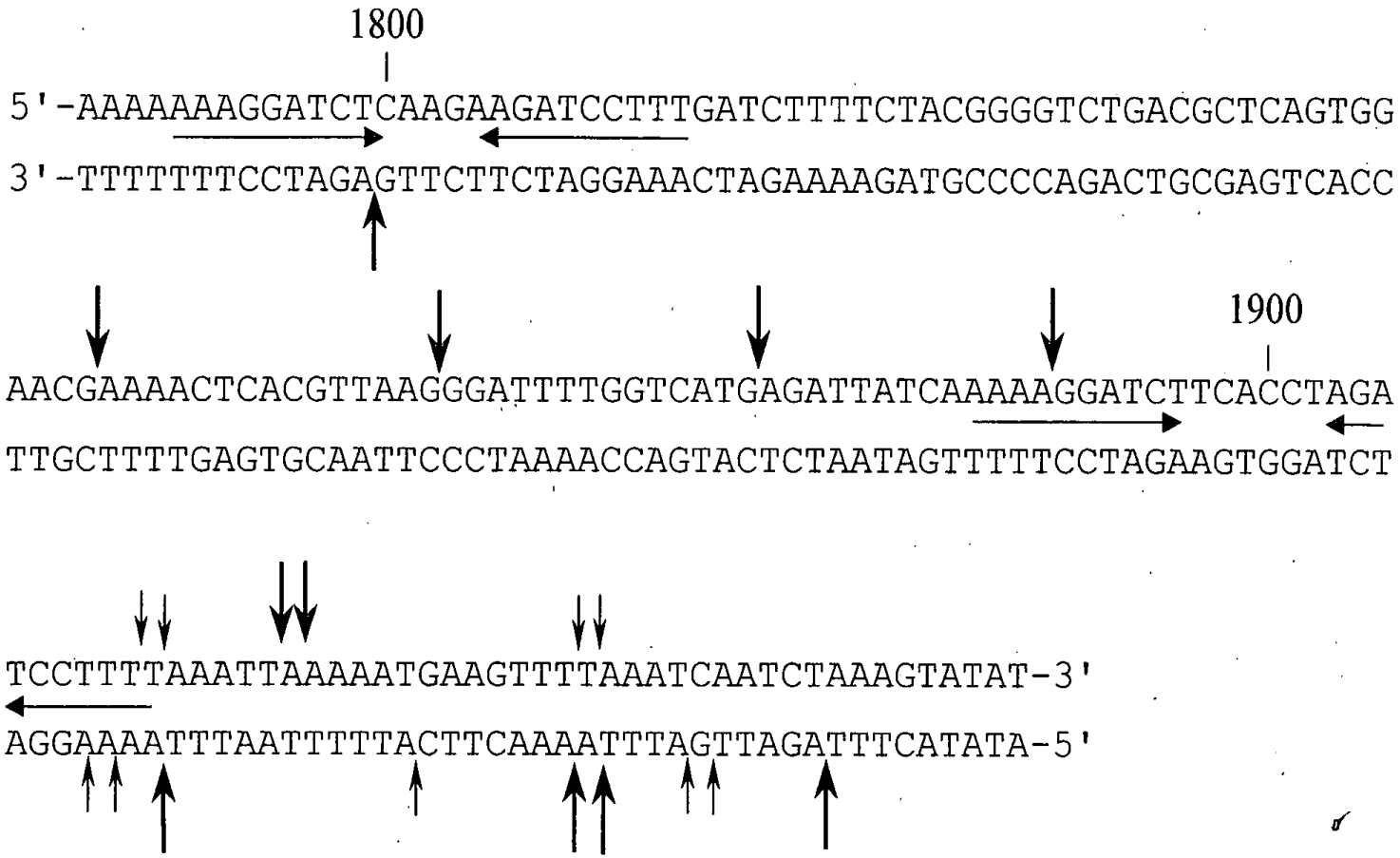

1800
5'-AAAAAAAGGATCTCAAGAAGATCCTTTGATCTTTTCTACGGGGTCTGACGCTCAGTGG
3'-TTTTTTTCCTAGAGTTCTTCTAGGAAACTAGAAAAGATGCCCCAGACTGCGAGTCACC
1900
AACGAAAACTCACGTTAAGGGATTTTGGTCATGAGATTATCAAAAAGGATCTTCACCTAGA
TTGCTTTTGAGTGCAATTCCCTAAAACCAGTACTCTAATAGTTTTTCCTAGAAGTGGATCT
TCCTTTTAAATTAAAAATGAAGTTTTAAATCAATCTAAAGTATAT-3'
AGGAAAATTTAATTTTTACTTCAAAATTTAGTTAGATTTCATATA-5'

Fig. 12A Fig. 12B Fig. 12C

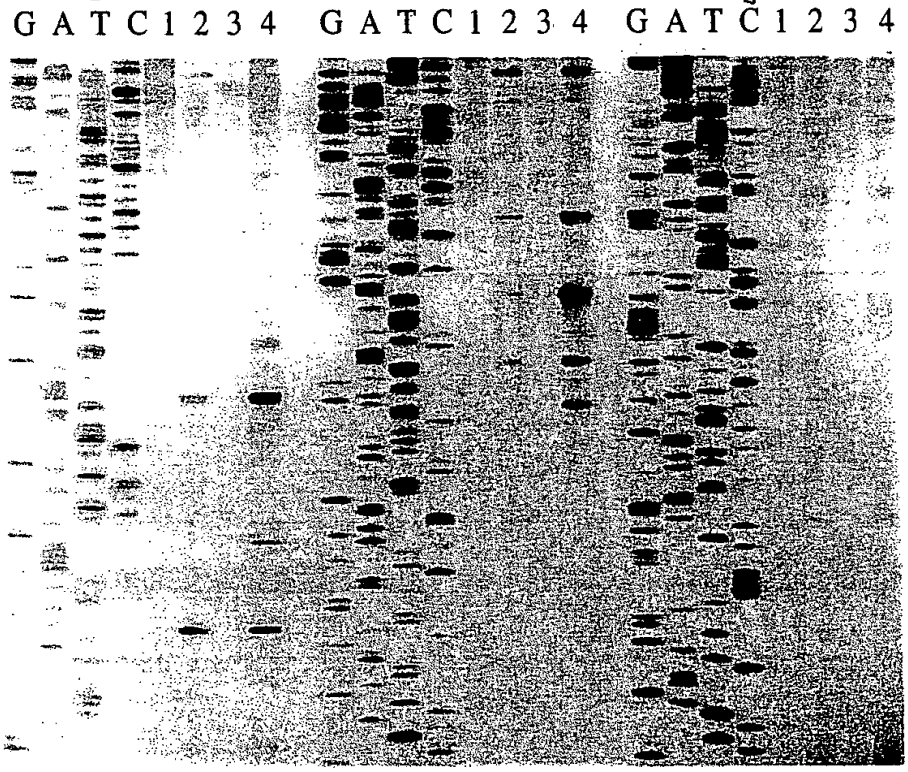


FIG. 13

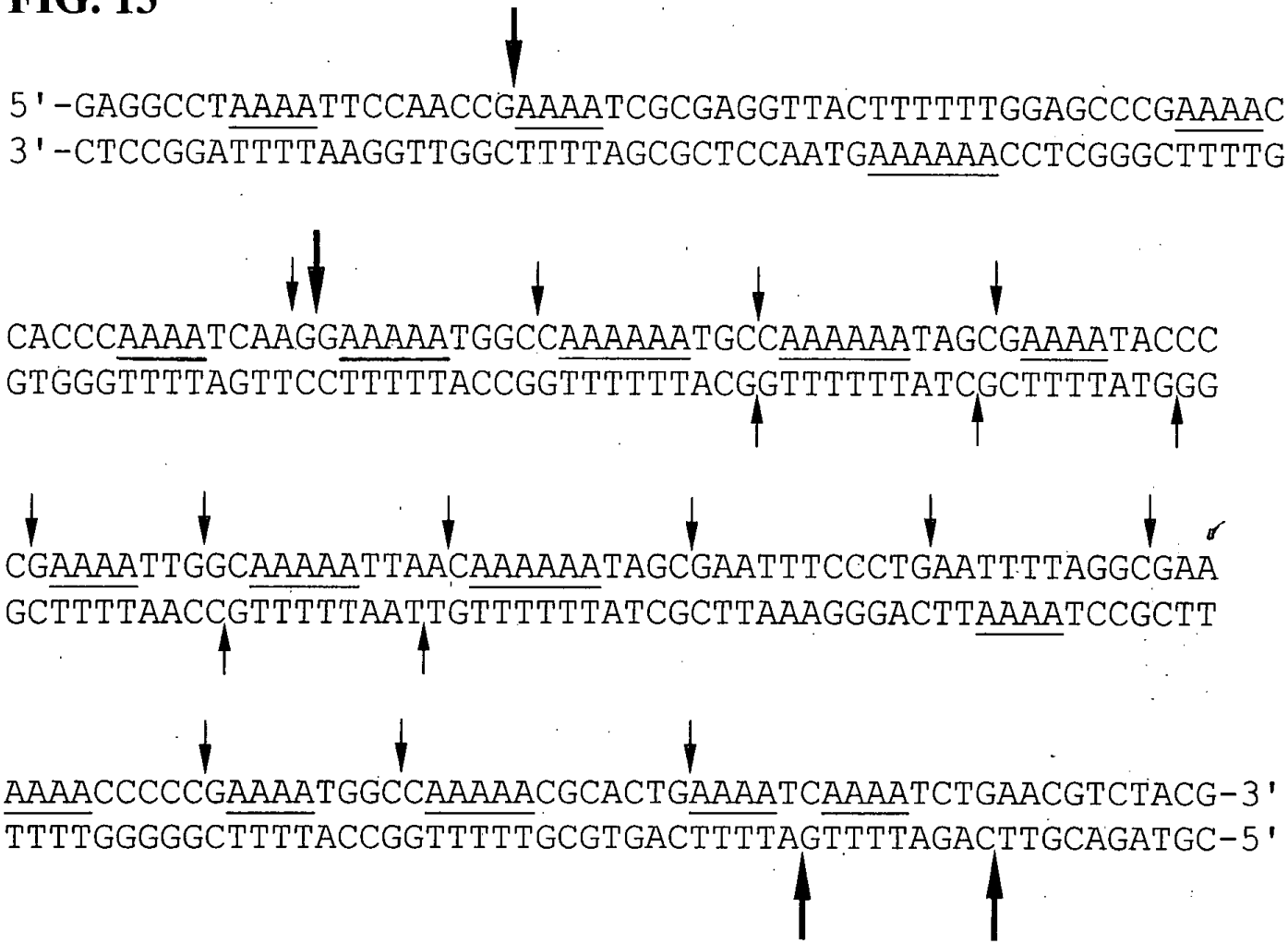

5'-GAGGCCTAAAATTCCAACCGAAAATCGCGAGGTTACTTTTTTGGAGCCCGAAAAC
3'-CTCCGGATTTTAAGGTTGGCTTTTAGCGCTCCAATGAAAAAACCTCGGGCTTTTG
CACCCAAAATCAAGGAAAAATGGCCAAAAAATGCCAAAAAATAGCGAAAATACCC
GTGGGTTTTAGTTCCTTTTTACCGGTTTTTTACGGTTTTTTATCGCTTTTATGGG
CGAAAATTGGCAAAAATTAACAAAAAATAGCGAATTTCCCTGAATTTTAGGCGAA
GCTTTTAACCGTTTTTAATTGTTTTTTATCGCTTAAAGGGACTTAAAATCCGCTT
AAAACCCCCGAAAATGGCCAAAAACGCACTGAAAATCAAAATCTGAACGTCTACG-3'
TTTTGGGGGCTTTTACCGGTTTTTGCGTGACTTTTAGTTTTAGACTTGCAGATGC-5'

FIG. 14A

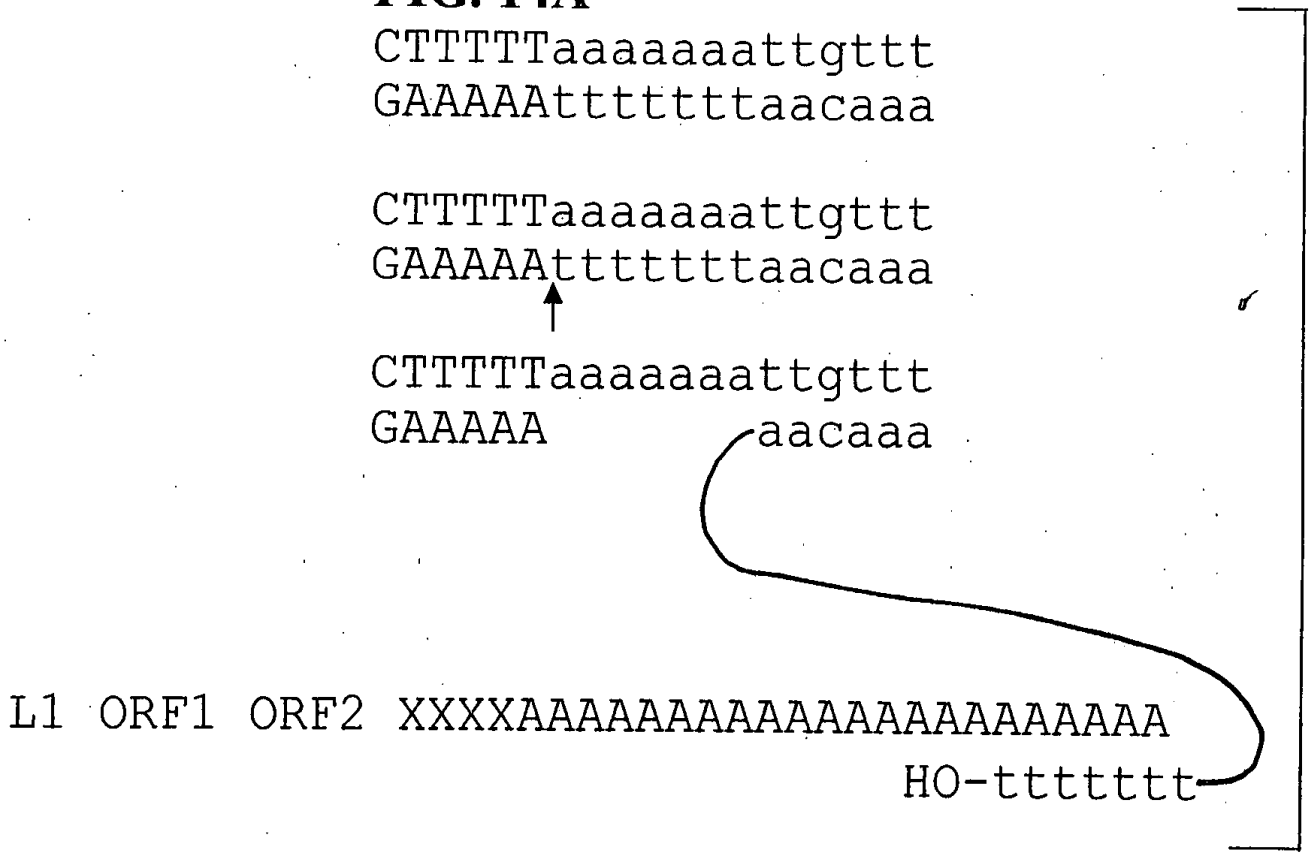

CTTTTTaaaaaaattgttt
GAAAAAttttttaacaaa
CTTTTTaaaaaaattgttt
GAAAAAttttttaacaaa
CTTTTTaaaaaaattgttt
GAAAAA
aacaaa
L1 ORF1 ORF2 XXXXAAAAAAAAAAAAAAAAAAAAAA
HO-ttttttt

FIG. 14Bii

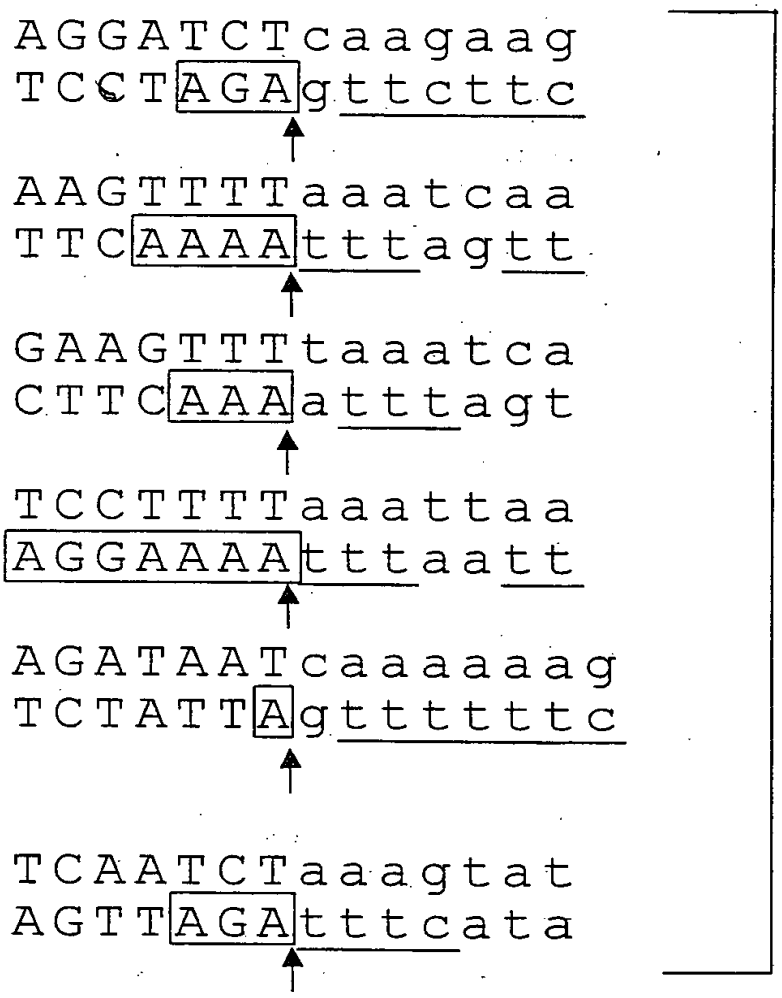

AGGATCTcaagaag
TCCTAGAgttcttc
AAGTTTTaaatcaa
TTCAAAAtttagtt
GAAGTTTtaaatca
CTTCAAAatttagt
TCCTTTTaaattaa
AGGAAAAtttaatt
AGATAATcaaaaaag
TCTATTAgttttttc
TCAATCTaaagtat
AGTTAGAtttcata

FIG. 14Bi

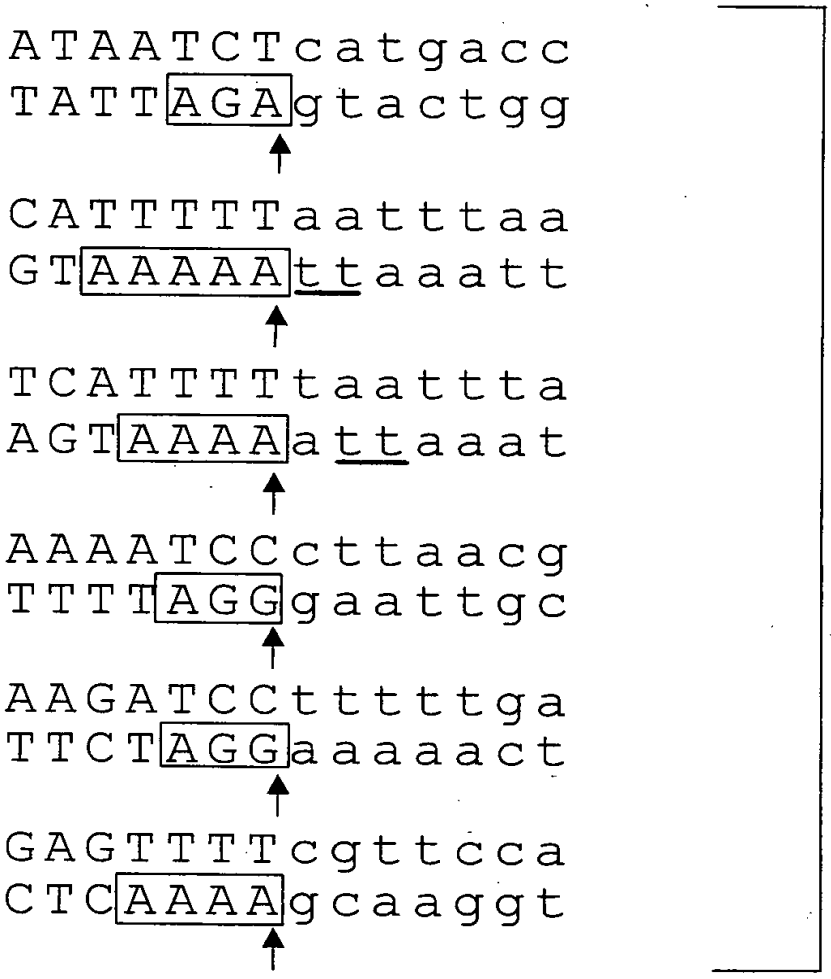

ATAATCTcatgacc
TATTAGAgtactgg
CATTTTTaatttaa
GTAAAAAttaaatt
TCATTTTtaattta
AGTAAAAattaaat
AAAATCCcttaacg
TTTTAGGgaattgc
AAGATCCttttttga
TTCTAGGaaaaact
GAGTTTTcgttcca
CTCAAAAgcaaggt

FIG. 14C

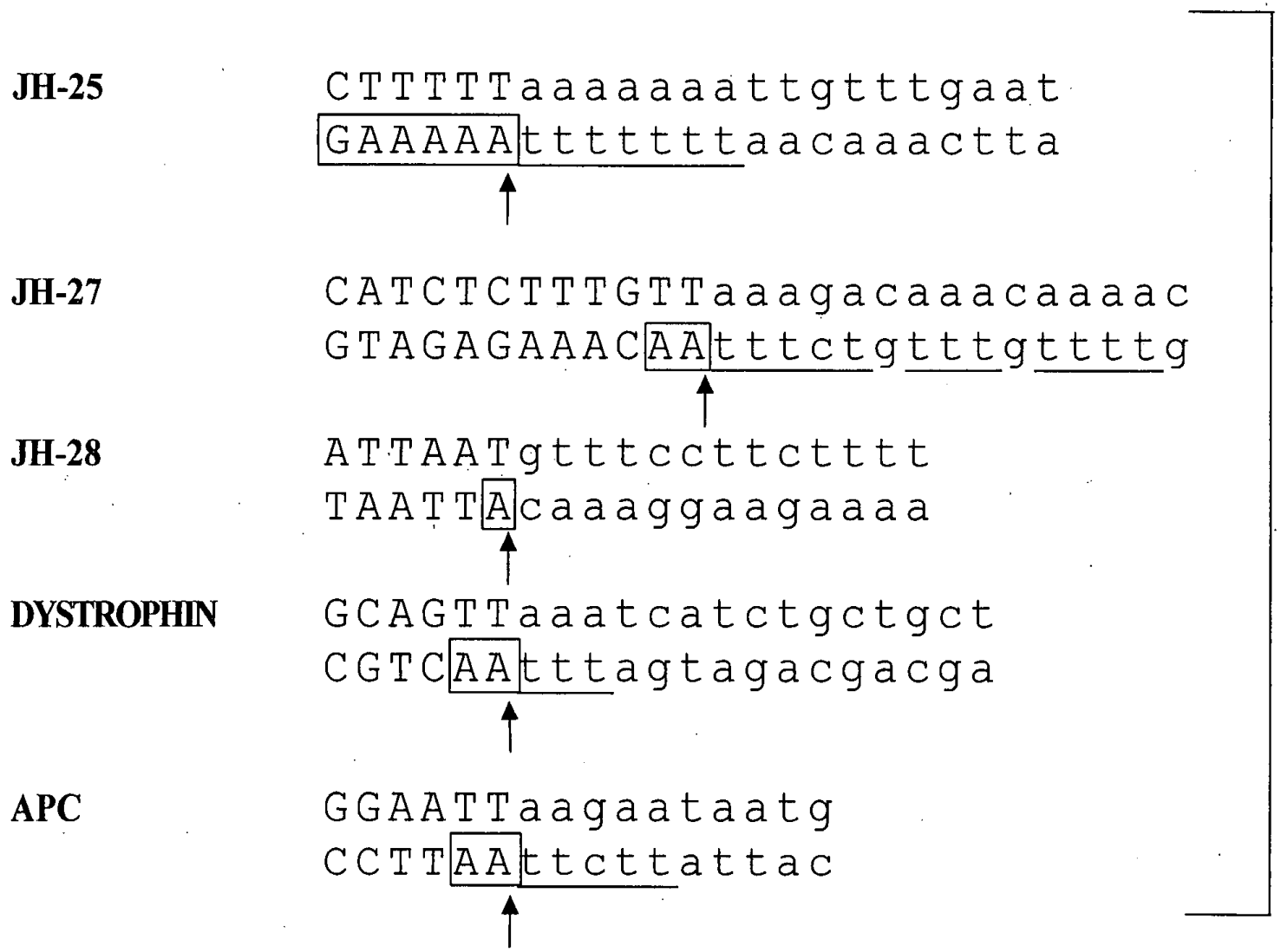

JH-25
CTTTTTaaaaaaaattgtttgaat
GAAAAAttttttttaacaaactta
JH-27
CATCTCTTTGTTaaagacaaacaaaac
GTAGAGAAACAAtttctgtttgttttg
JH-28
ATTAATgtttccttctttt
TAATTAcaaaggaagaaaa
DYSTROPHIN
GCAGTTaaatcatctgctgct
CGTCAAtttagtagacgacga
APC
GGAATTaagaataatg
CCTTAAttcttattac

FIG. 14D

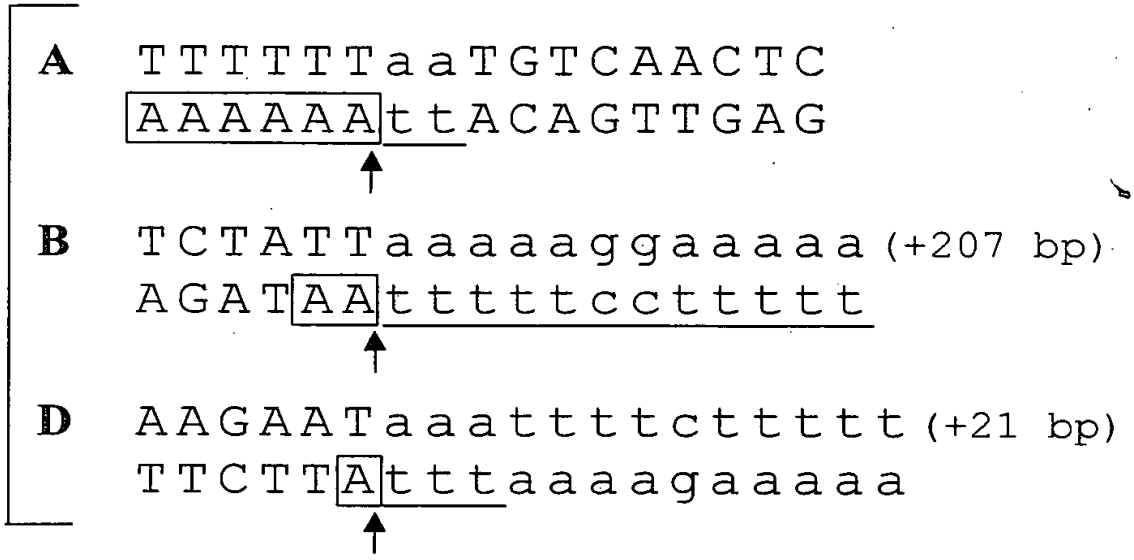


FIG. 14E

FIG. 14F

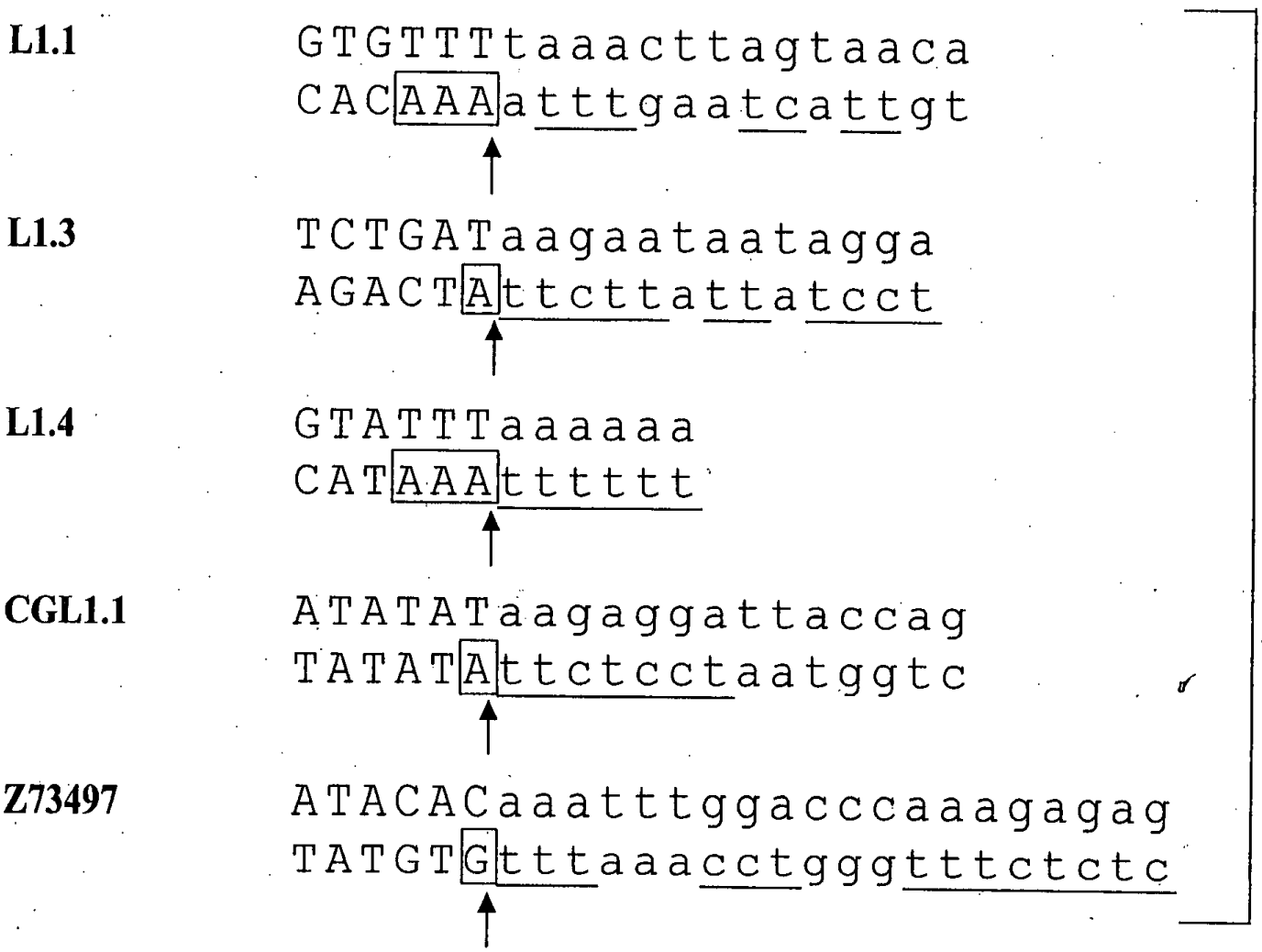

L1.1
GTGTTTtaaacttagtaaca
CACAAAatttgaatcattgt
L1.3
TCTGATaagaataatagga
AGACTAttcttattatcct
L1.4
GTATTTaaaaaa
CATAAAtttttt
CGL1.1
ATATATaagaggattaccag
TATATAttctcctaatggtc
Z73497
ATACACaaatttggacccaaagagag
TATGTGtttaaacctgggtttctctc

FIG. 14G

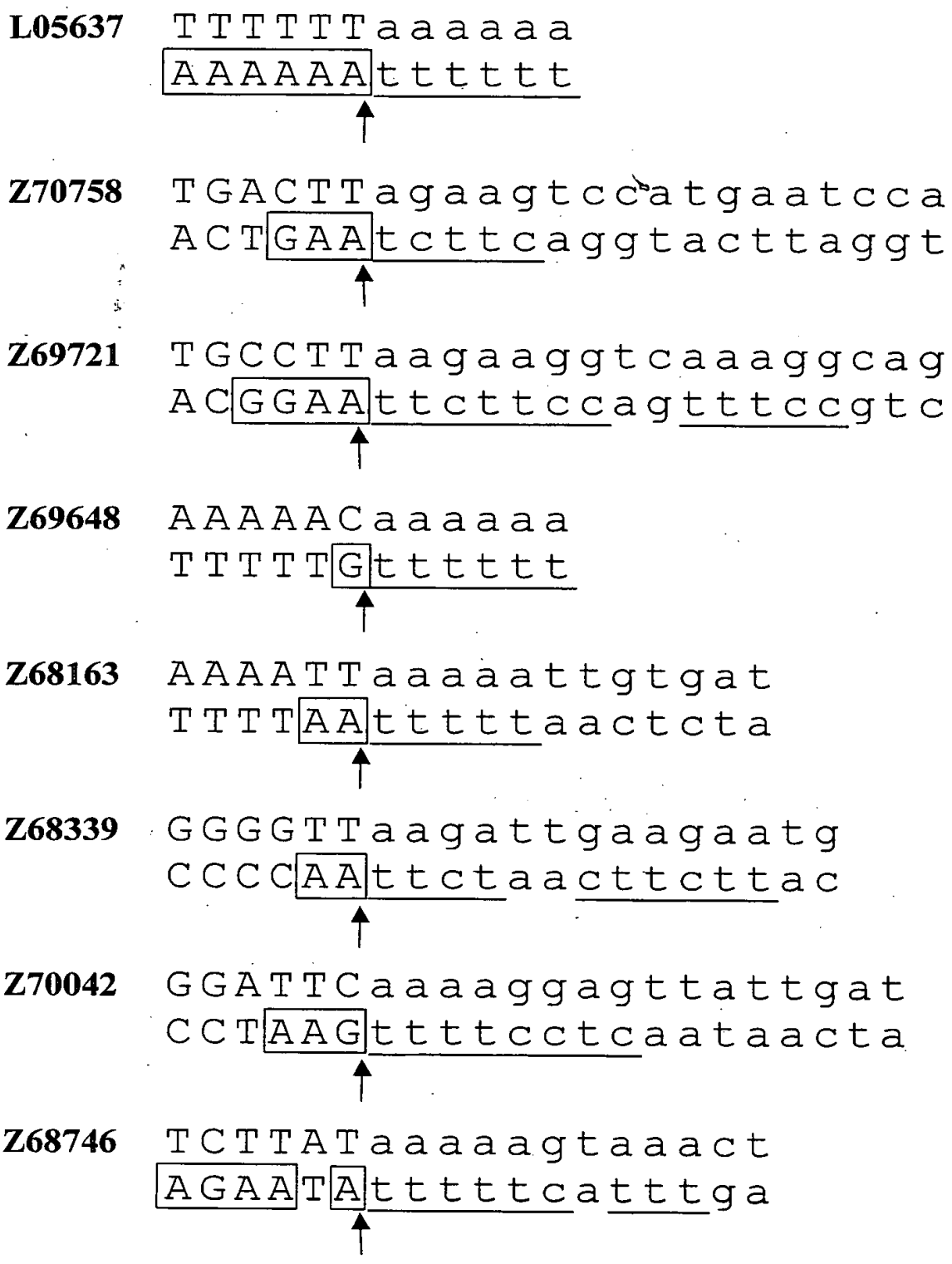
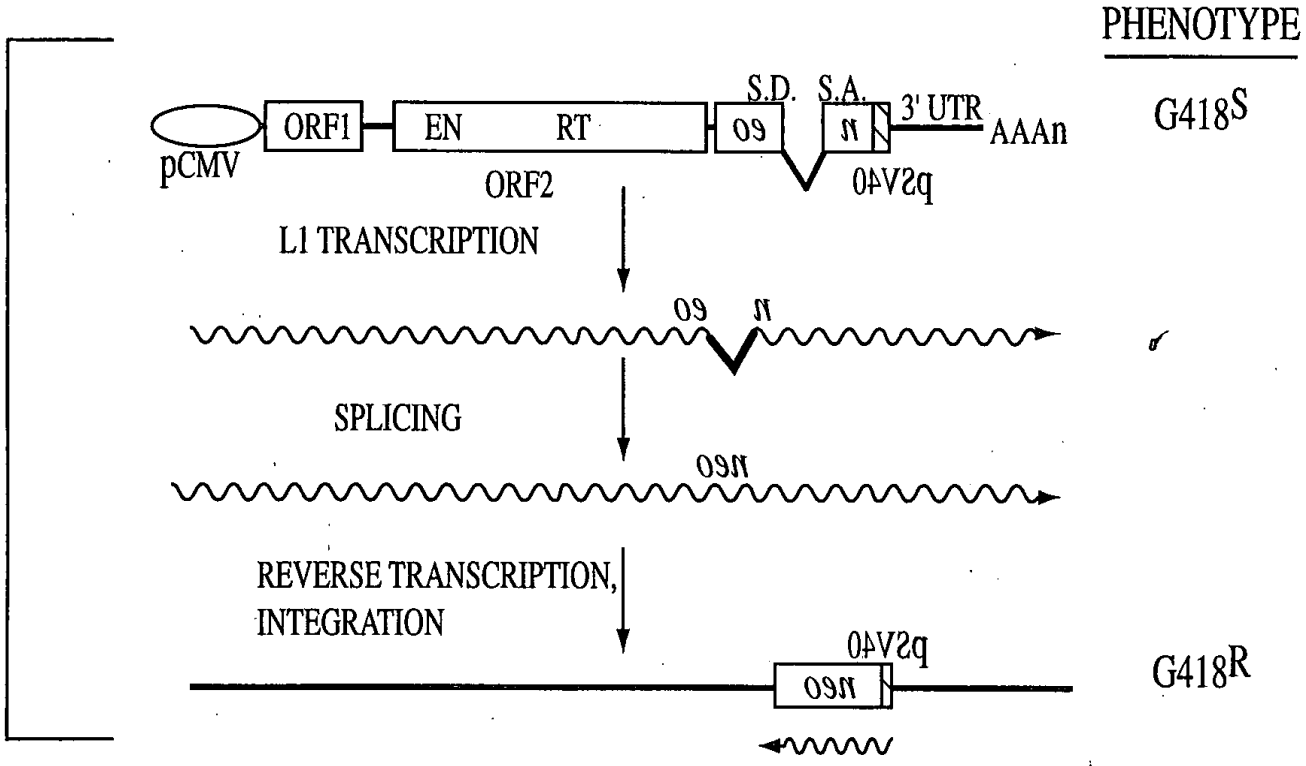

L05637
TTTTTTaaaaaa
AAAAAAtttttt
Z70758
TGACTTagaagtccatgaatcca
ACTGAAtcttcaggtacttaggt
Z69721
TGCCTTaagaaggtcaaaggcag
ACGGAAttcttccagtttccgtc
Z69648
AAAAACaaaaaa
TTTTTGtttttt
Z68163
AAAATTaaaaattgtgat
TTTTAAttttttaactcta
Z68339
GGGGTTaagattgaagaatg
CCCCAAttctaacttcttac
Z70042
GGATTCaaaaggagttattgat
CCTAAGttttcctcaataacta
Z68746
TCTTATaaaaagtaaact
AGAATAttttttcatttga

Fig. 15A


PHENOTYPE
pCMV
ORF1
EN
RT
S.D.
S.A.
3' UTR
AAAn
ORF2
L1 TRANSCRIPTION
SPLICING
REVERSE TRANSCRIPTION,
INTEGRATION
G418S
G418R

CONSTRUCT	TRANSPOSITION FREQUENCY (10^{-6} $cell^{-1}$)
WILDTYPE L1	335
D703Y (RT^-)	0.5
N14 (EN^-)	3.4
D145A (EN^-)	1.0
D205G (EN^-)	0.7
H230A (EN^-)	1.3

FIG. 15B

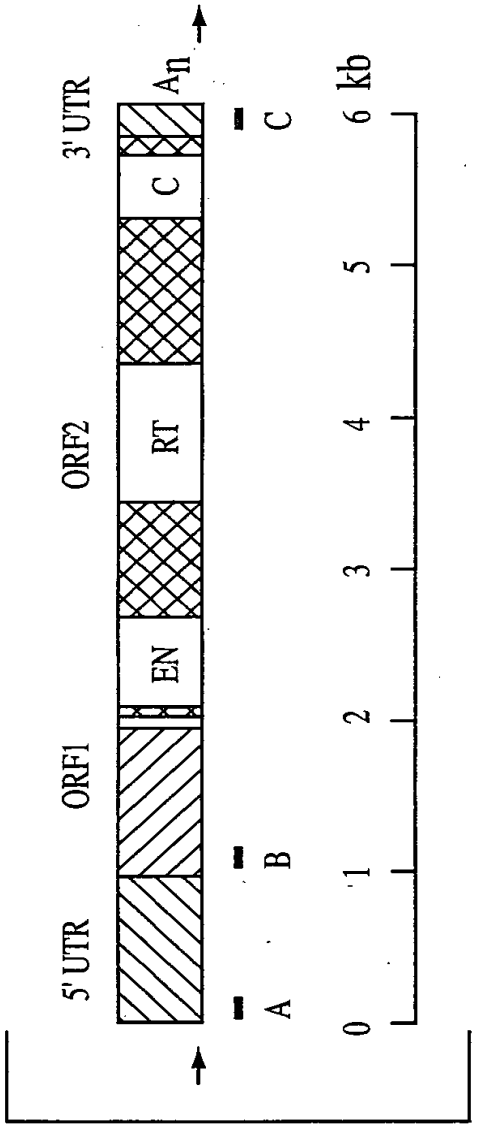


Fig. 16

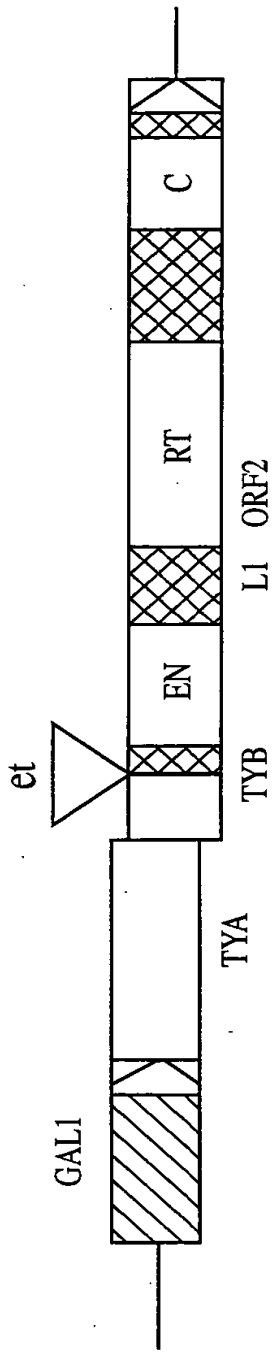


Fig. 17A

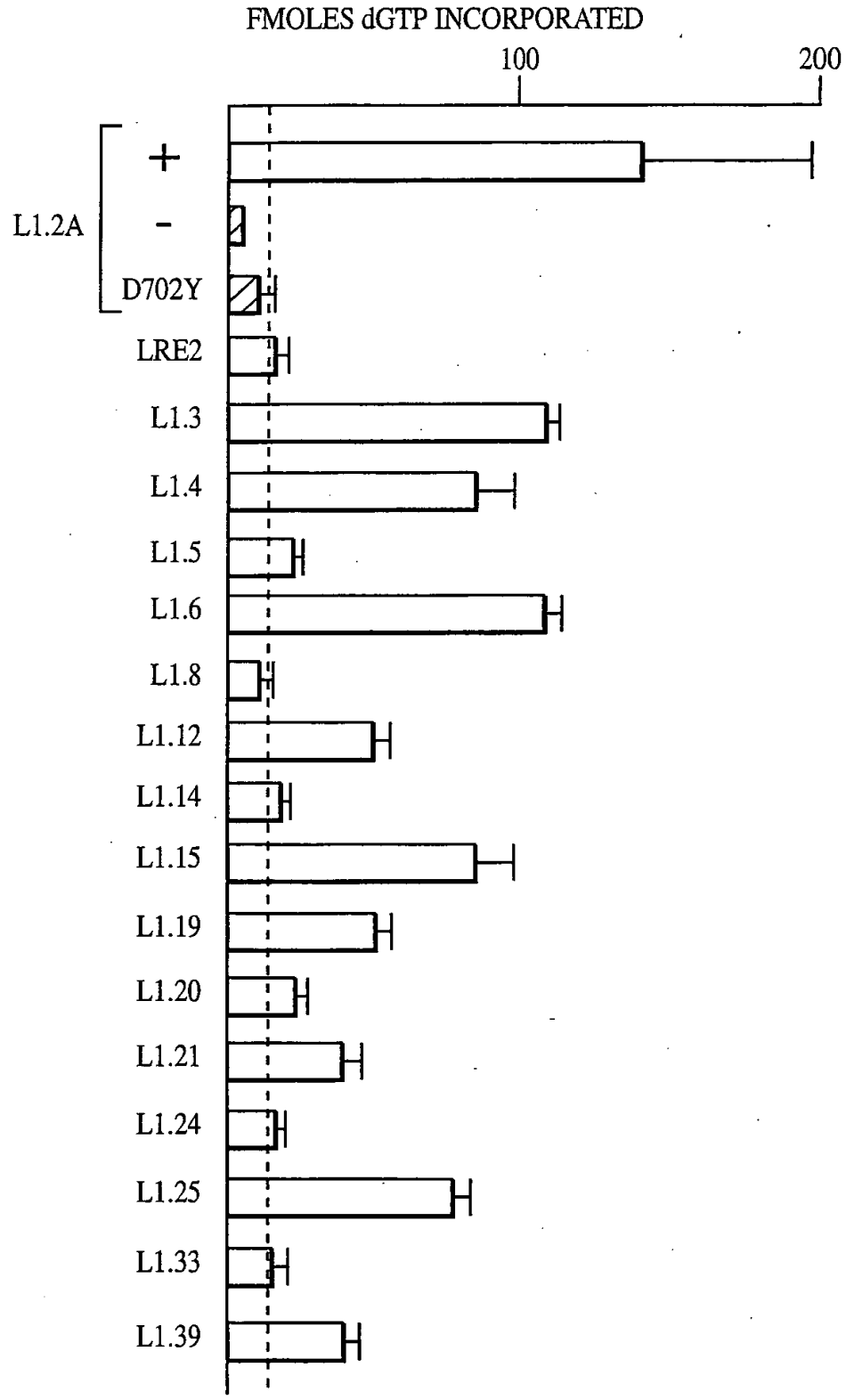

FMOLES dGTP INCORPORATED
100
200
L1.2A
+
-
D702Y
LRE2
L1.3
L1.4
L1.5
L1.6
L1.8
L1.12
L1.14
L1.15
L1.19
L1.20
L1.21
L1.24
L1.25
L1.33
L1.39

Fig. 17B

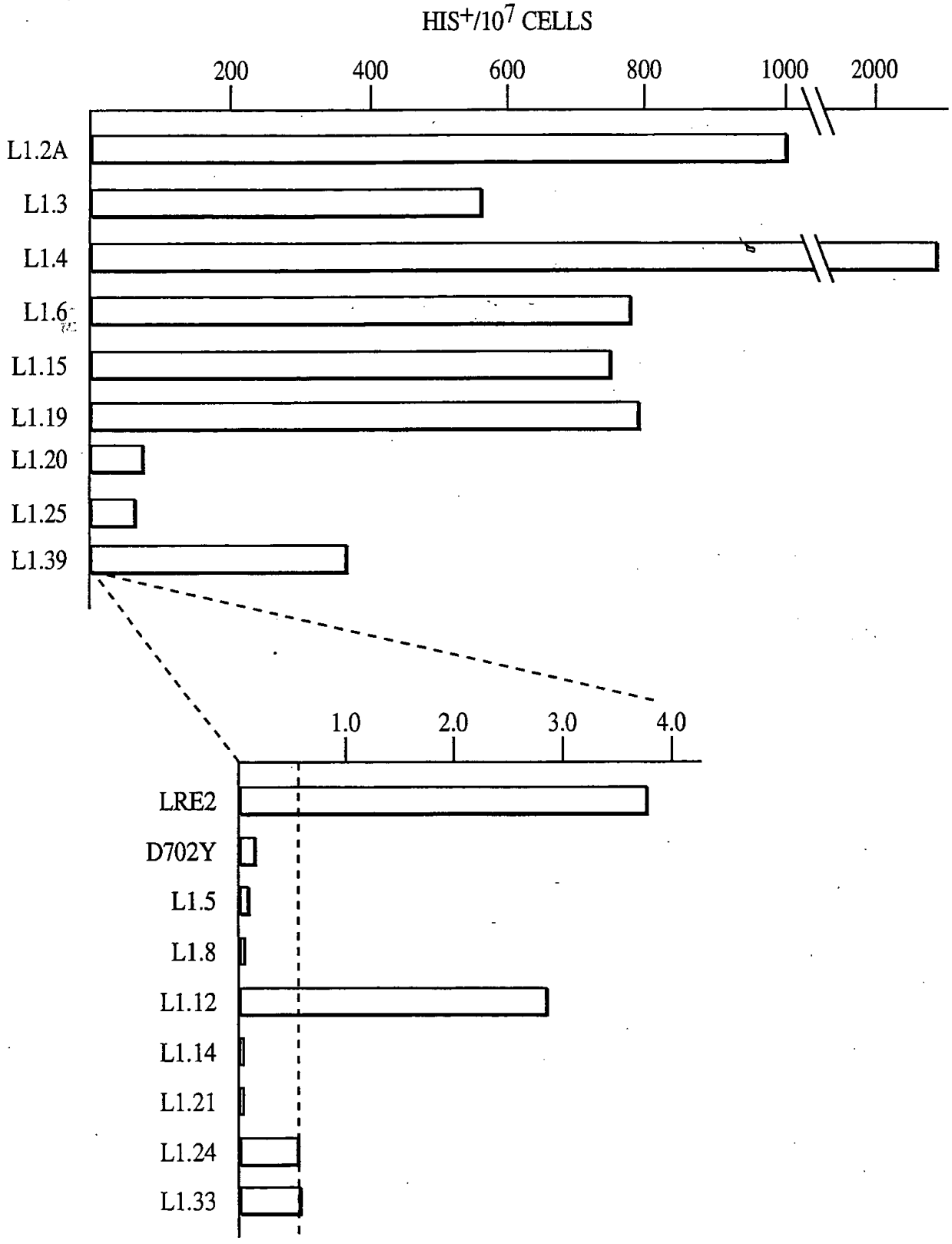
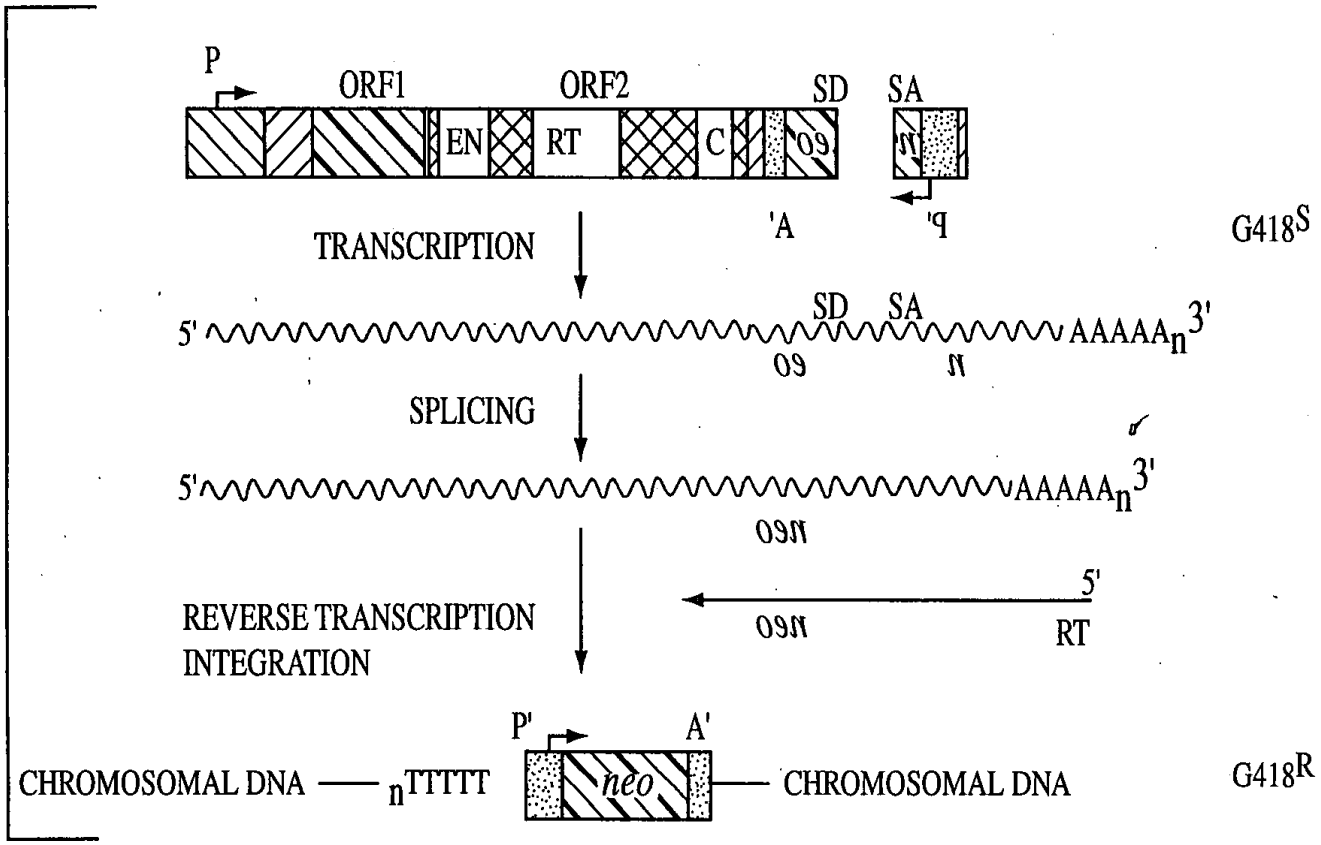

HIS+/10^7 CELLS
200
400
600
800
1000
2000
L1.2A
L1.3
L1.4
L1.6
L1.15
L1.19
L1.20
L1.25
L1.39
1.0
2.0
3.0
4.0
LRE2
D702Y
L1.5
L1.8
L1.12
L1.14
L1.21
L1.24
L1.33

Fig. 17C

Fig. 18A


P
ORF1
ORF2
SD
SA
EN
RT
C
TRANSCRIPTION
G418S
5'
AAAAAn3'
SPLICING
REVERSE TRANSCRIPTION
INTEGRATION
5'
RT
P'
A'
CHROMOSOMAL DNA
nTTTTT
neo
CHROMOSOMAL DNA
G418R

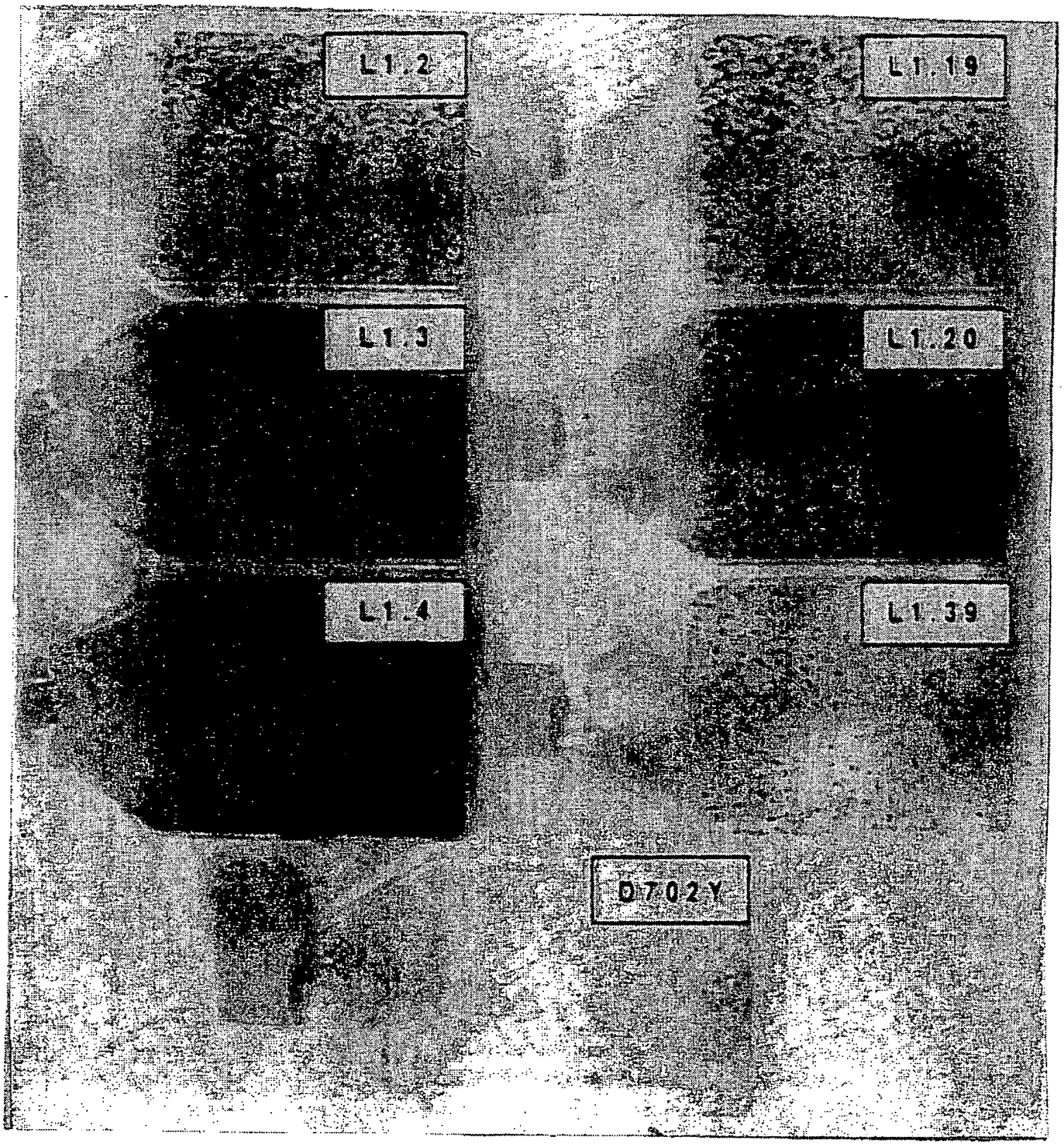


FIG. 18B